Armed Forces College of Medicine

AFCM

Functions of Cell mediated immunity&

Self MHC molecules

Dr.Alaa Ahmed Aly

Professor of Microbiology & Immunology

ILOs of Immunogens,Antigens & Self molecules

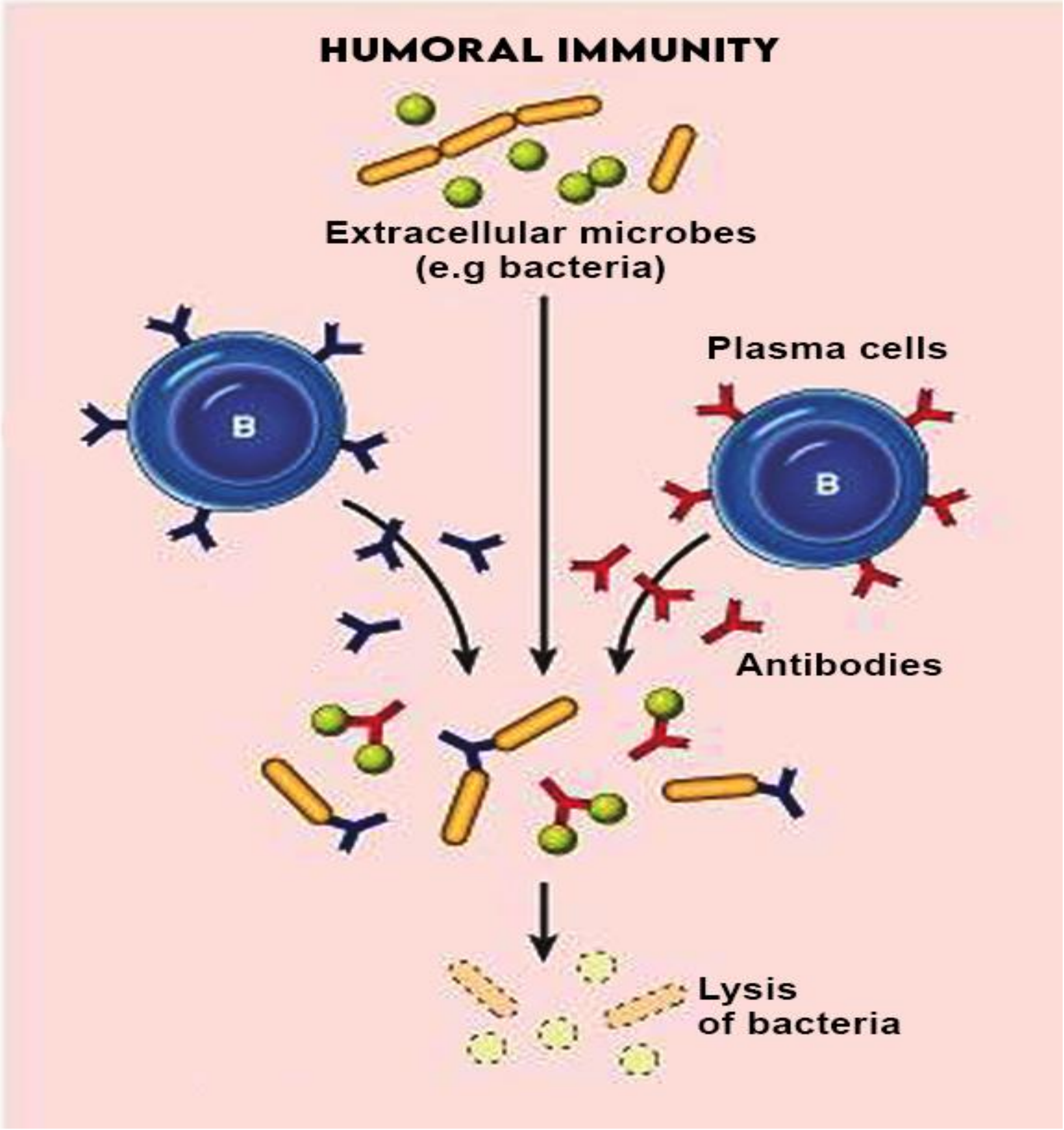
By the end of this lecture the student will be able to:

1. Outline series of reactions and functions of cell mediated immunity
2. Compare between MHC class I and II regarding structure , function and importance in health
3. Discuss steps of development of T lymphocytes in thymus.

Humoral Immunity

- Mediated by **Abs** produced by **activated B cells** (**plasma** cells)

Eliminate extracellular microbes & toxins



Cell mediated immunity

Mediated by

activated T cels

Functions of Cell mediated immunity

Elimination of Intra cellular (IC) microbes

A) Elimination of IC microbes inaccessible to Abs

1) Few bacteria as Mycobacterium tuberculosis (M. TB)

Survive & replicate in phagocytes

↓

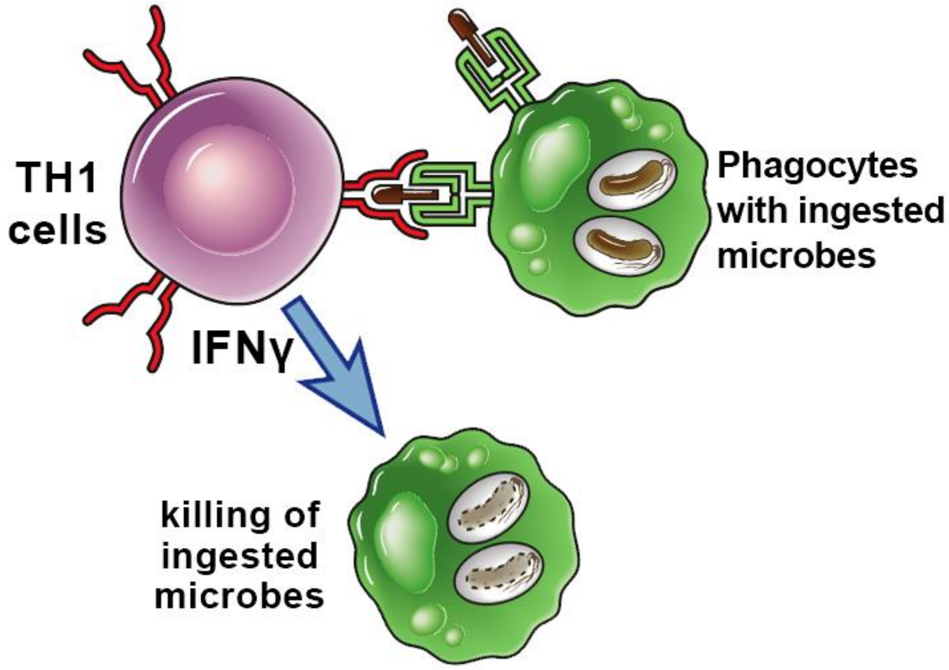
Phagocytes must be **activated by Interferon γ from T helper 1**

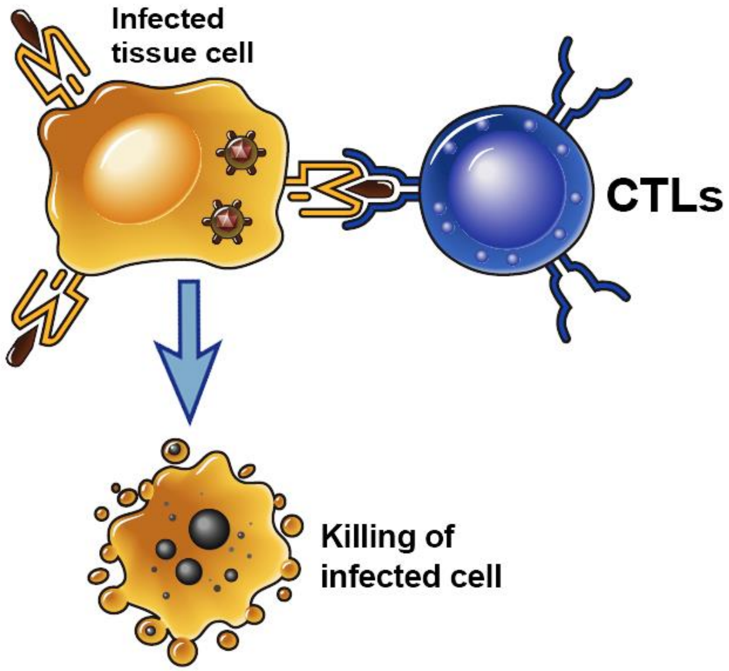
2) Viruses (obligate intracellular organisms)

Survive & replicate in non-phagocytic cells (tissue cells)

↓

These cells **must be killed by Cytotoxic T lymphocytes (CTLs)**


TH1 cells
Phagocytes with ingested microbes
IFNγ
killing of ingested microbes

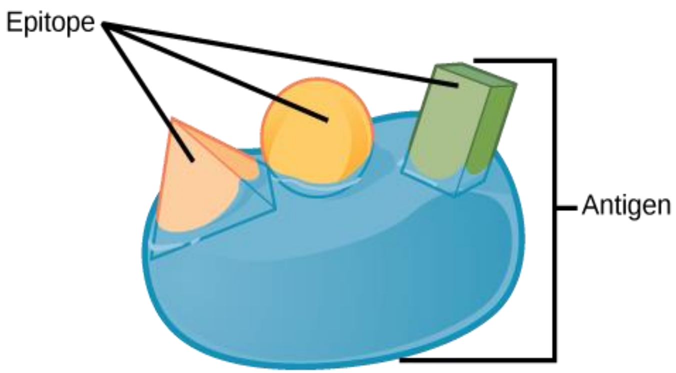


EPITOPE

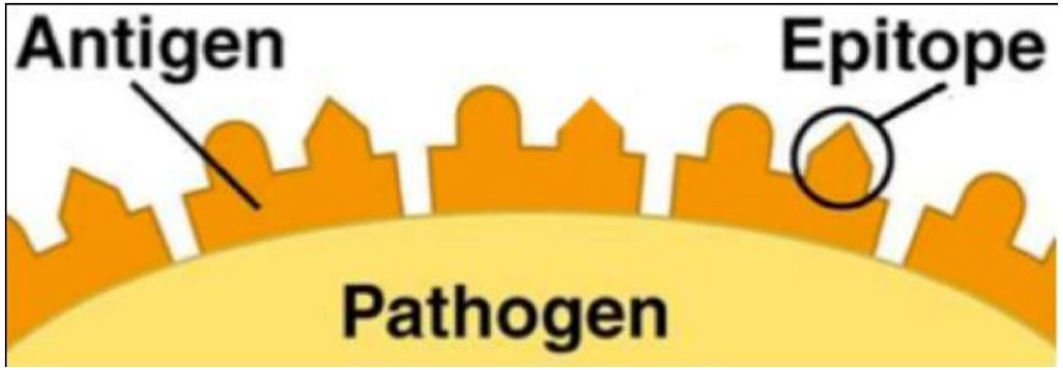
Definition The **smallest biochemical unit** of Antigen that binds specifically **with Ag receptor** on B & T lymphocytes

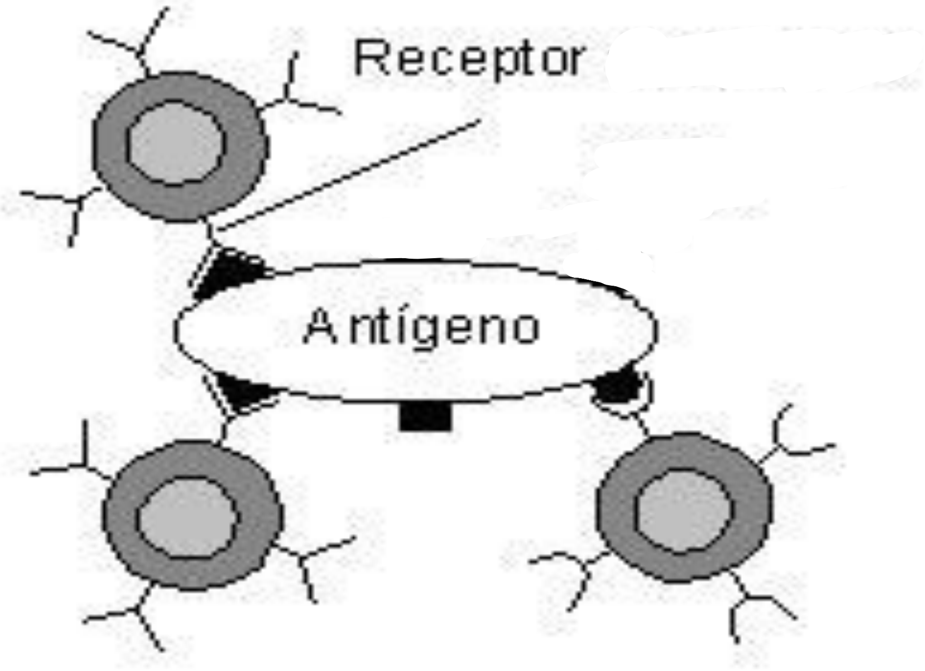
↓

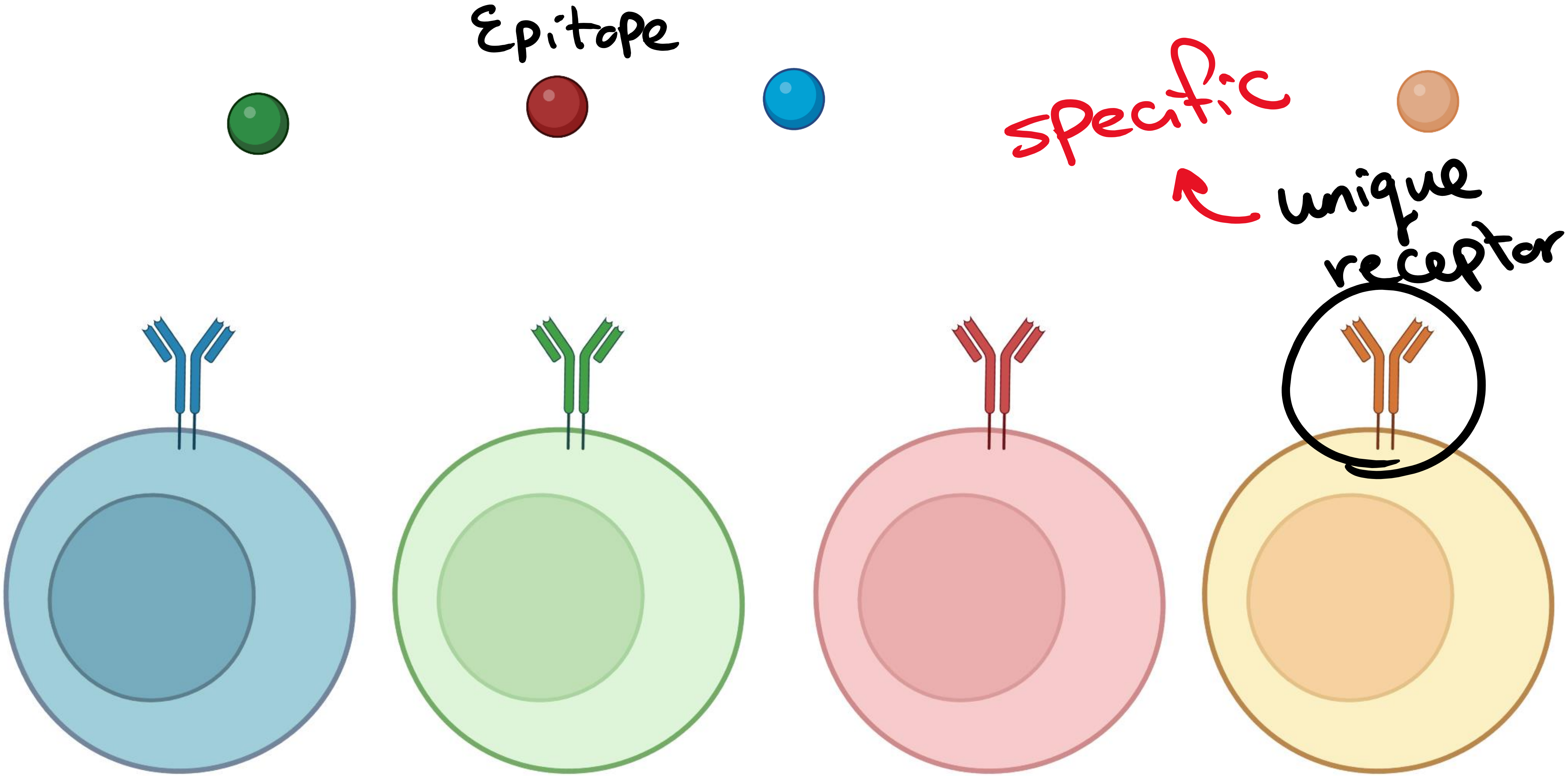
Stimulation of immune response



Each Ag possesses different epitopes



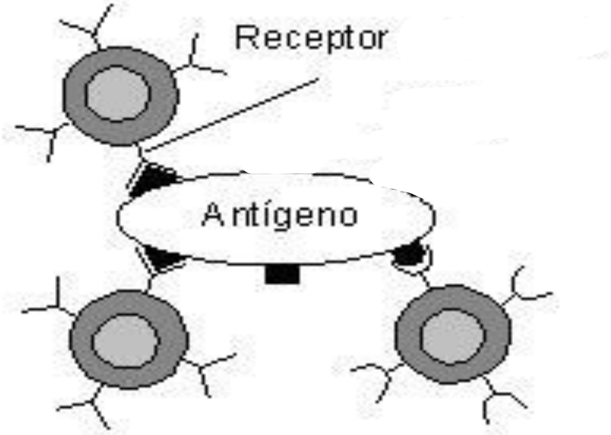




4 different clones

EPITOPE

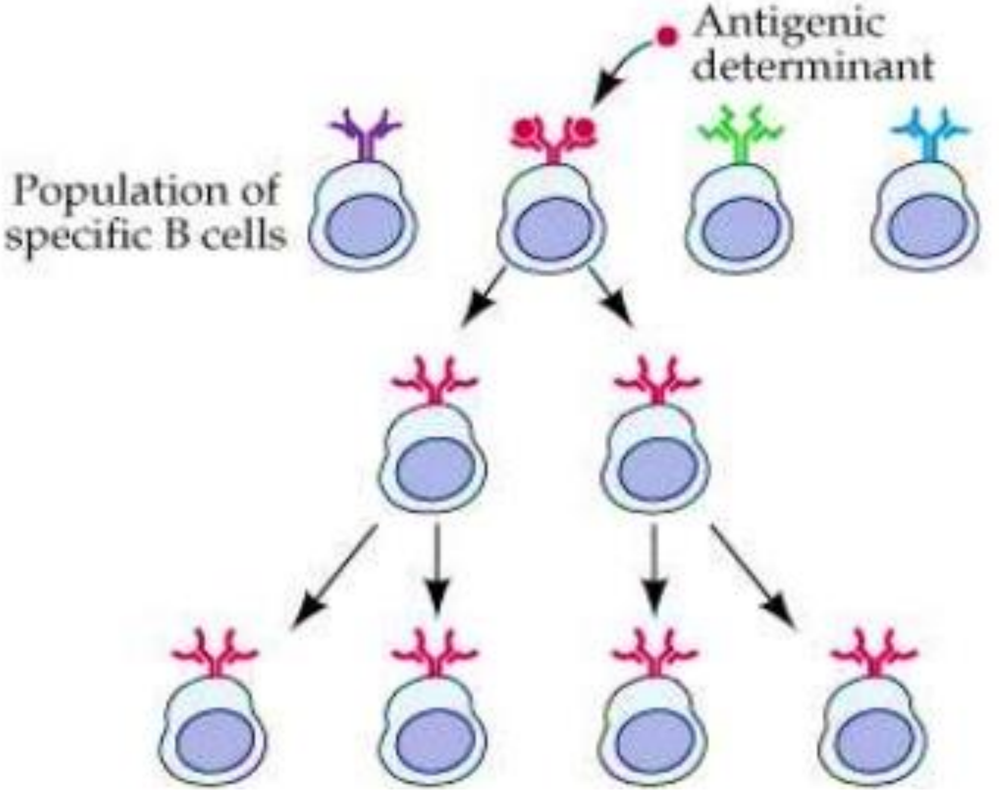
Importance



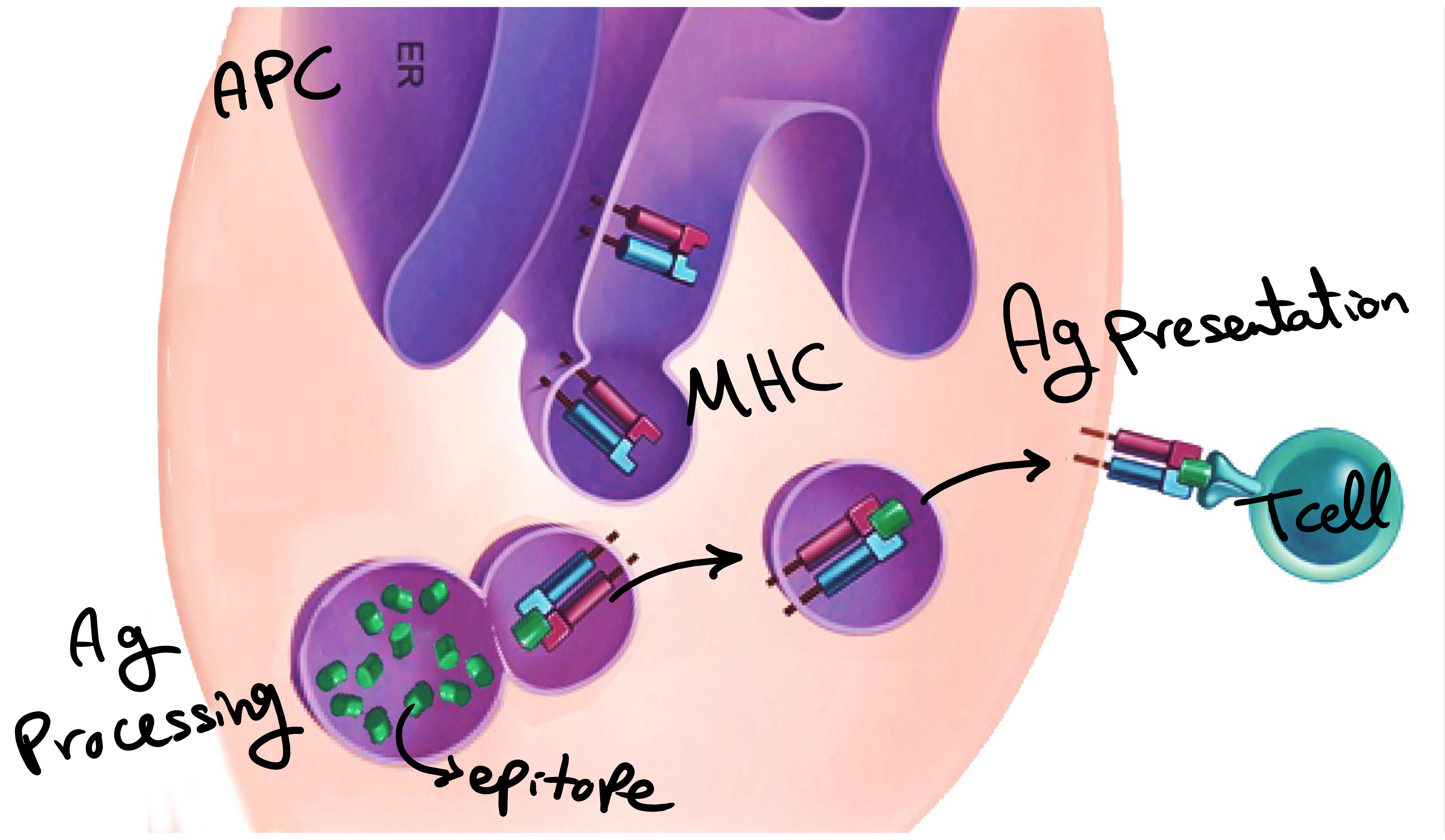
- **Each lymphocyte clone has a unique receptor that is:**

  a) **Specific** for a distinct epitope

  b) **Different** from receptors of all other clones



- **T & B lymphocyte receptors** recognize only **epitopes**

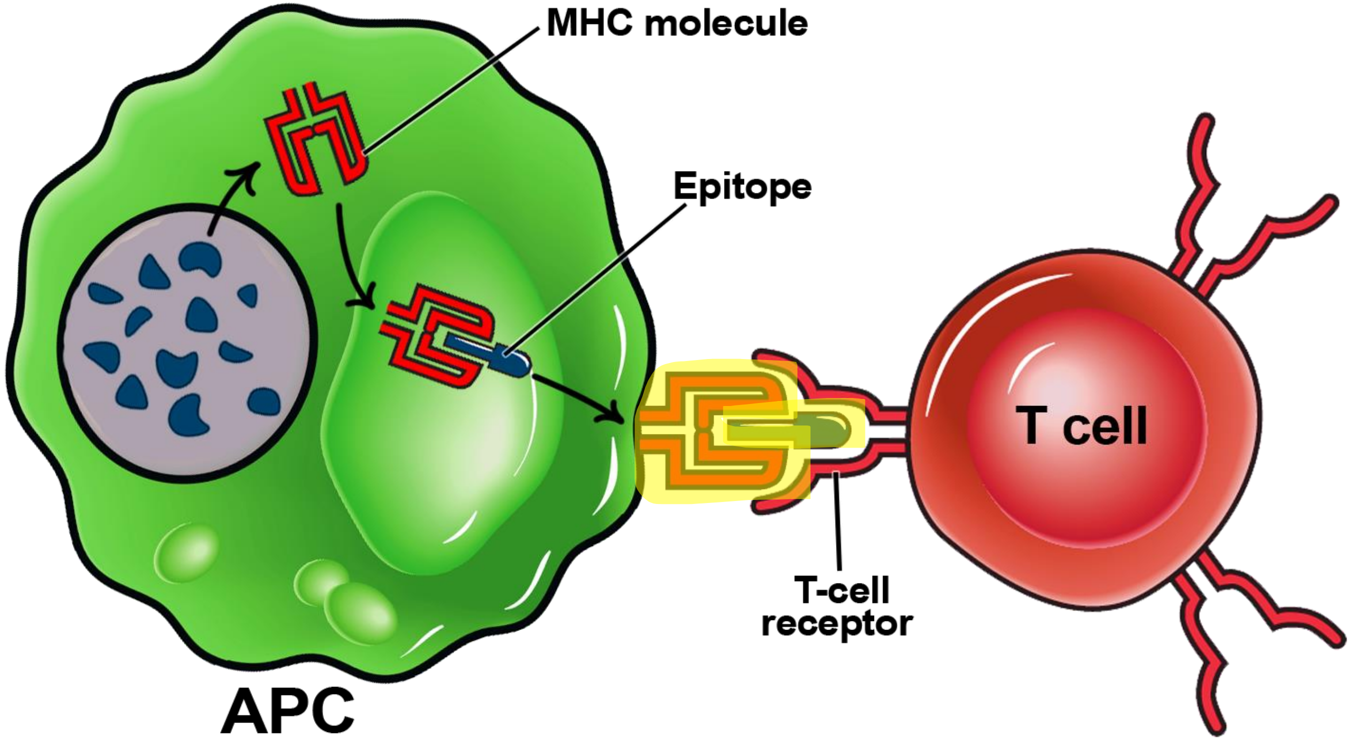

APC
ER
MHC
Ag Presentation
Tcell
Ag Processing
epitope

EPITOPE

Importance

▶ T lymphocyte receptor (TCR) only recognizes:

- Processed protein Ag (epitope) }
- in MHC molecule

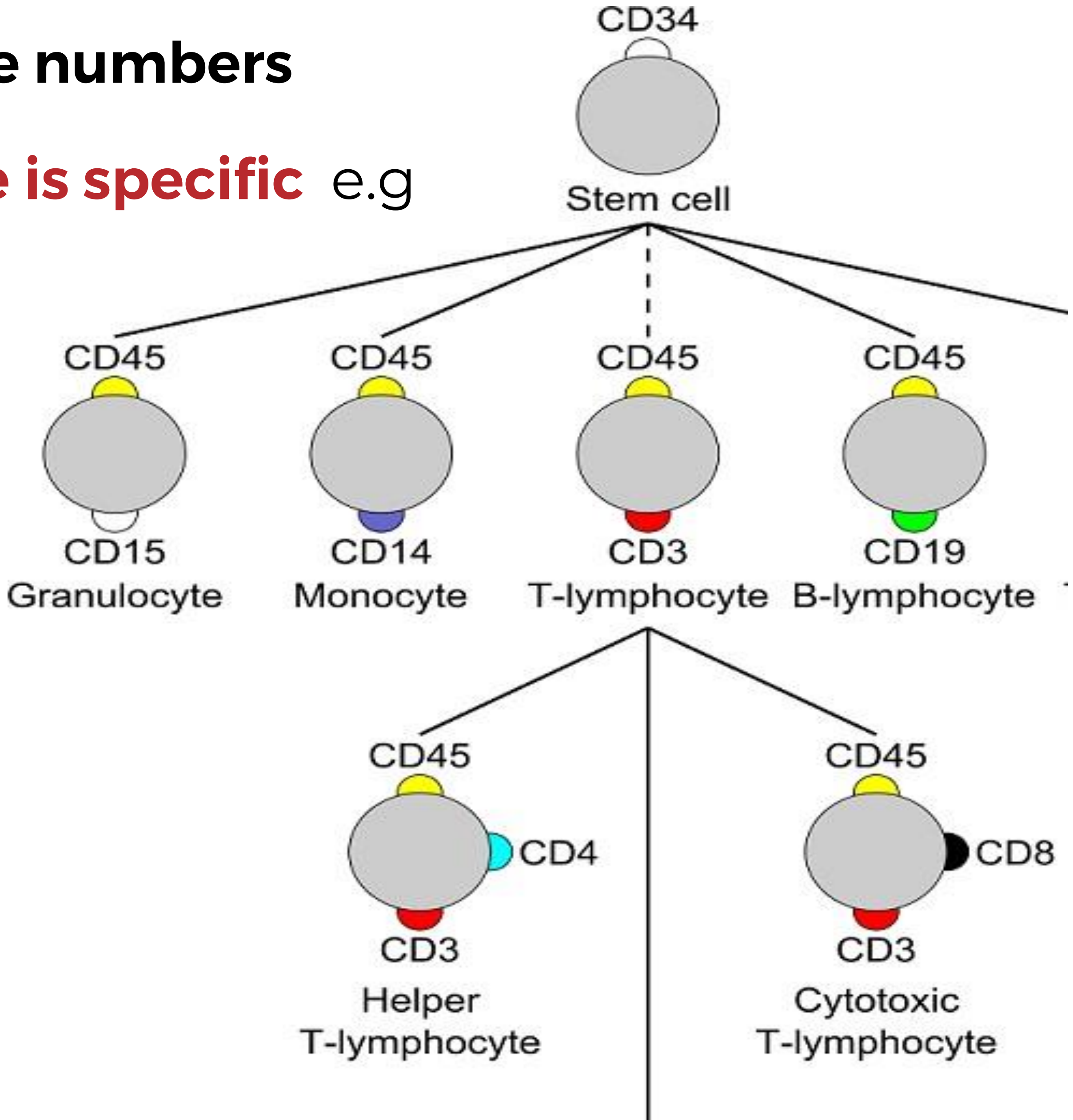


CD molecules

a) Expressed on **all immune cells & have numbers**

b) Each immune cell has **> 1 CD**, **but one is specific** e.g

T cells : CD3 {
- **Th : CD4**
- **Tc : CD8**

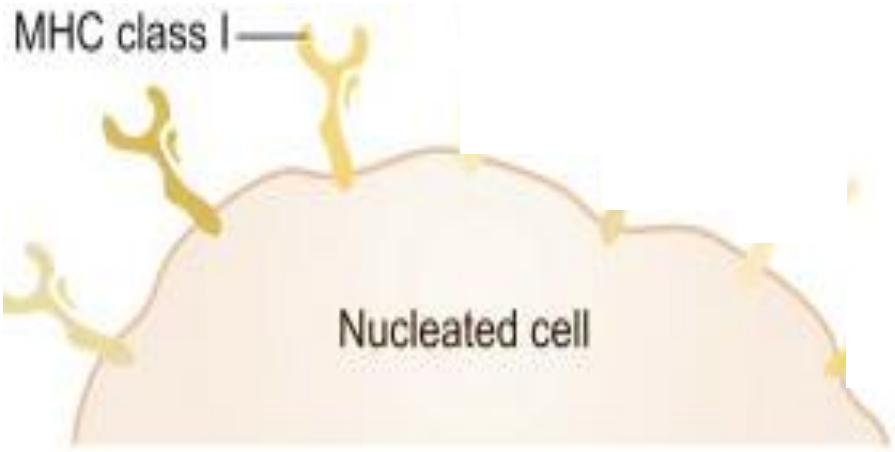


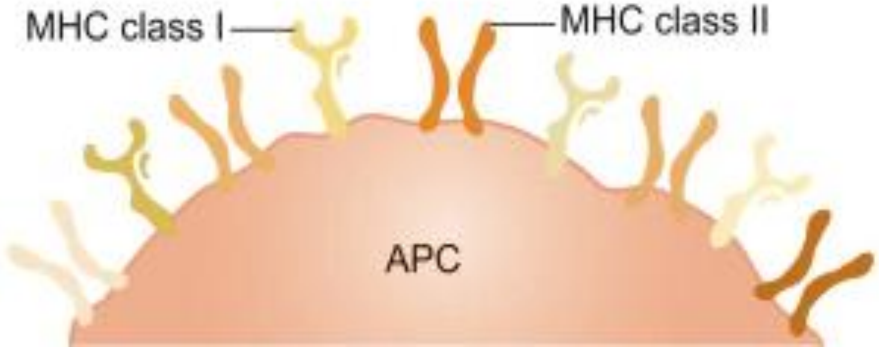
Major histocompatibility complex (MHC) OR Human leukocyte Ags (HLA)

Definition **self proteins** on **surface of nucleated cells** (**absent on RBCs**)

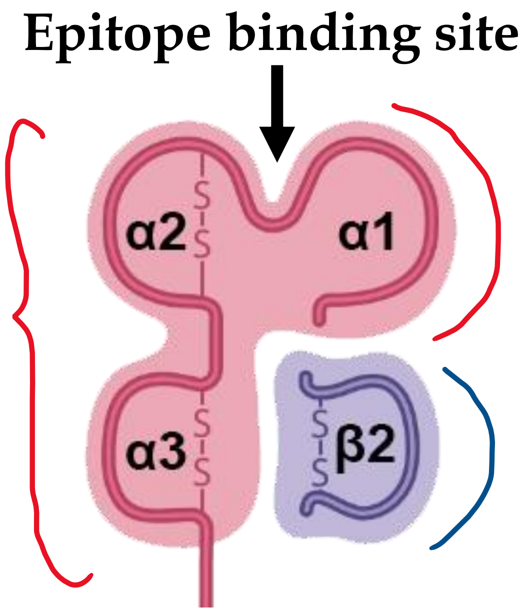
& were **1st discovered on leukocytes**

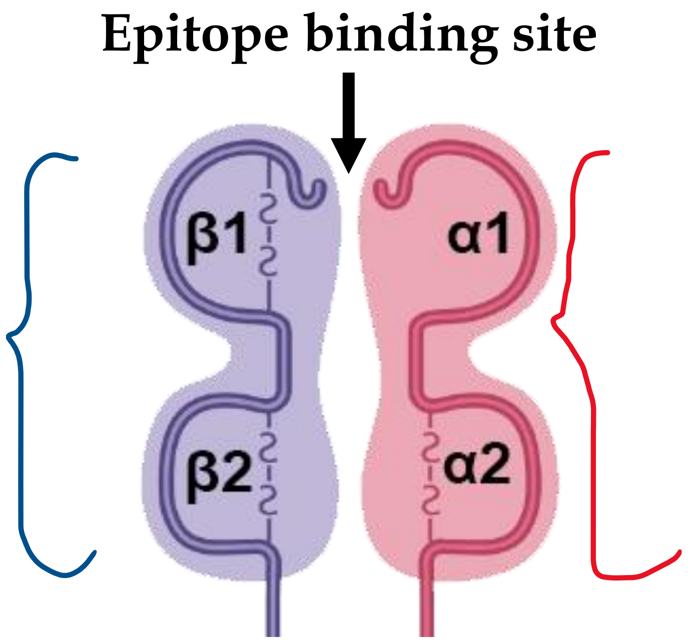
	MHC class I	MHC class II
Site	All nucleated cells **(including professional APCs)**	Professional APCs : **Dendritic cells, Macrophages & B cells**



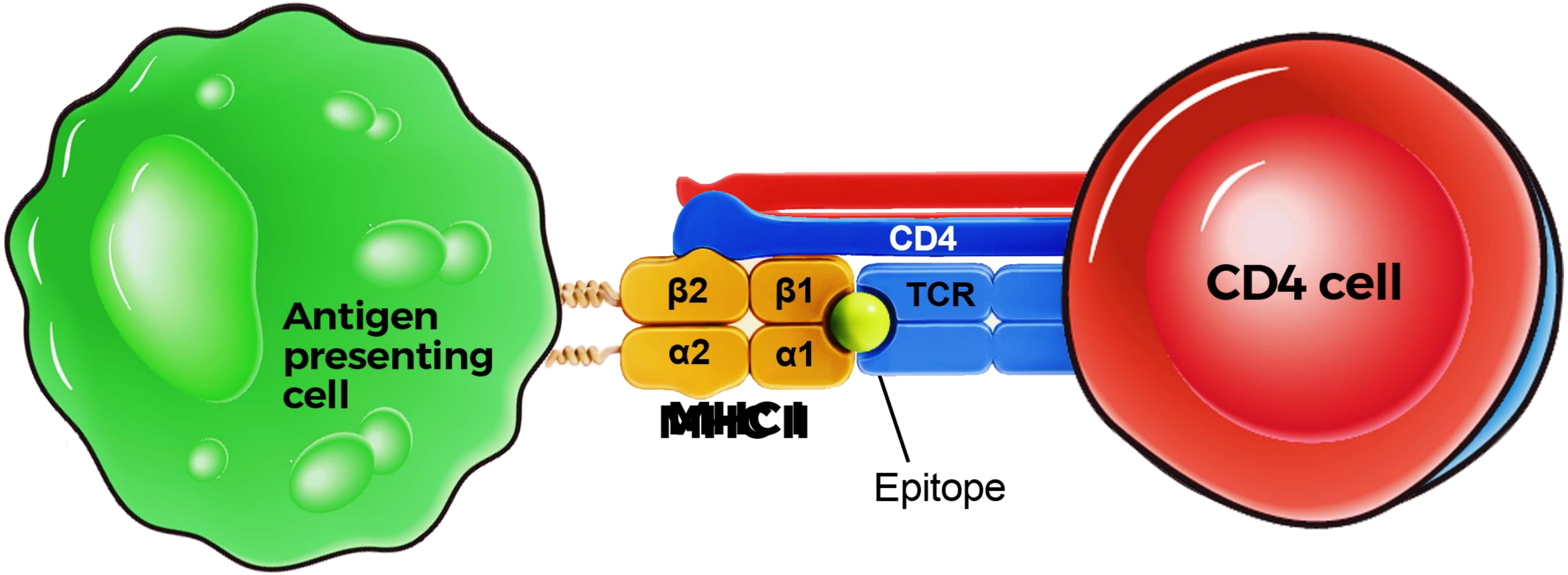


	MHC class I	MHC class II
Structure	Each molecule (protein) is formed of 2 polypeptide chains : α & β	
	Has an Ag (epitope) binding site	
Source of expressed Ag	Endogenously synthesized (new) Ags ?	Exogenously phagocytosed Ags ?





	MHC class I	MHC class II
Importance in health	**T cells recognize Ag only in association with MHC molecules**	
	Tc (CD8) cells: Recognize Ag only if associated with MHC **class I** molecule ↓ Recognized by T cell receptor (TCR) & **CD8** molecule	**Th (CD4) cells:** Recognize Ag only if associated with MHC **class II** molecule ↓ Recognized by T cell receptor (TCR) & **CD4** molecule



Armed Forces College of Medicine

T cell development

Dr. Alaa Ahmed Aly

Professor of Microbiology & Immunology

T lymphocytes development

I Origin of T lymphocytes

From lymphoid stem cells in bone marrow

⬇

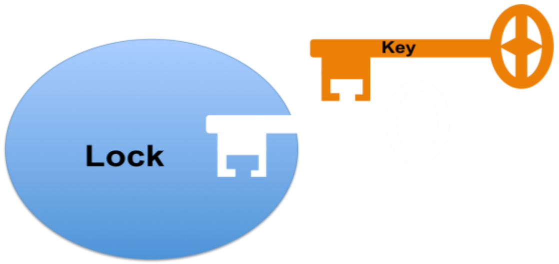
Immature thymocytes

⬇

Circulate in blood with no surface markers

II Stages of maturation

A Expression of T cell receptor (TCR) complex

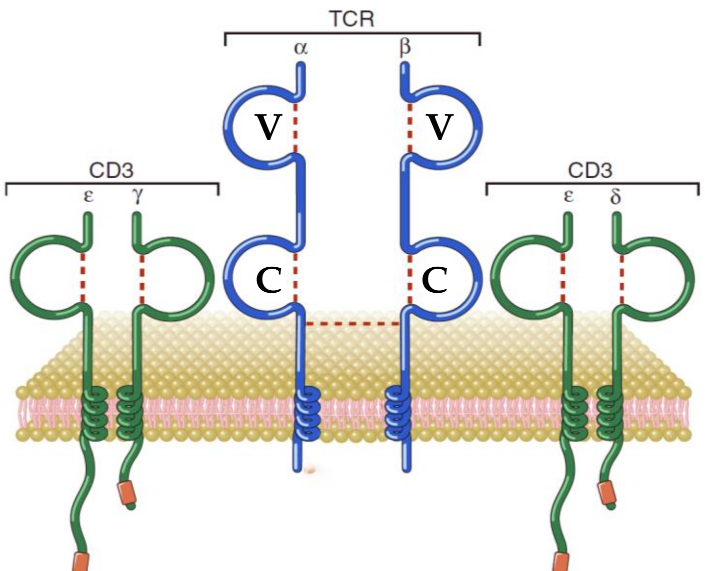


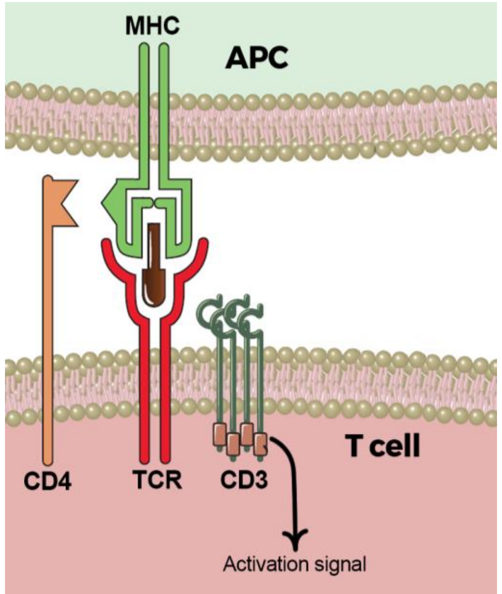
TCR Formed of **α & β polypeptide chains having**:

1) **C (constant) region**

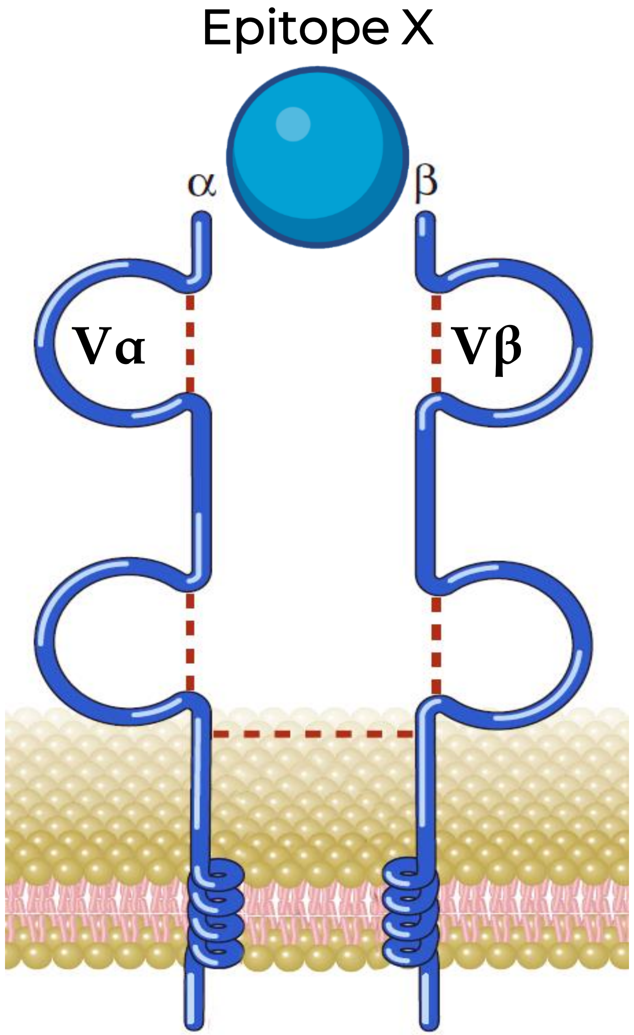
2) **V (variable) region** recognizes:
- **Specific peptide Ag (epitope):** (Complementary to it)
- **Part of MHC mol**

CD3 Associated with TCR ➜ **Transmits intracellular activation signal**

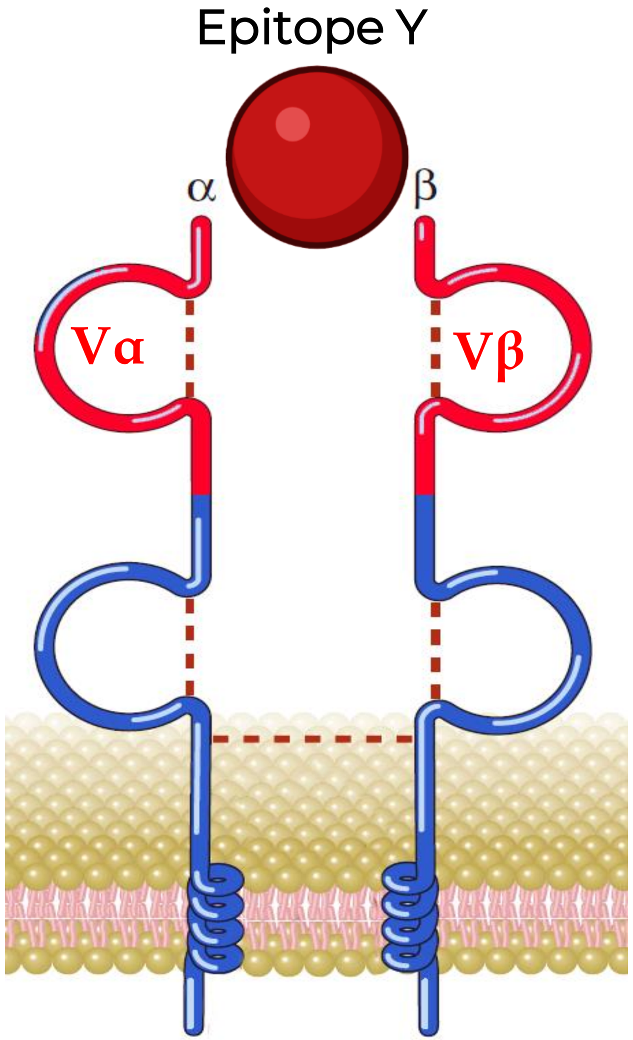




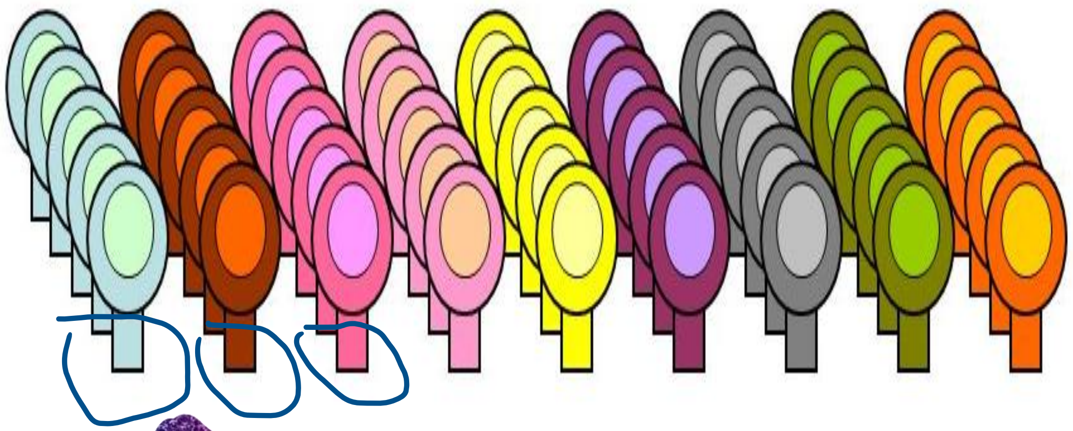
Diversity of TCR



Clone 1



Clone 2



Millions of different specific T clones

Diversity of TCR

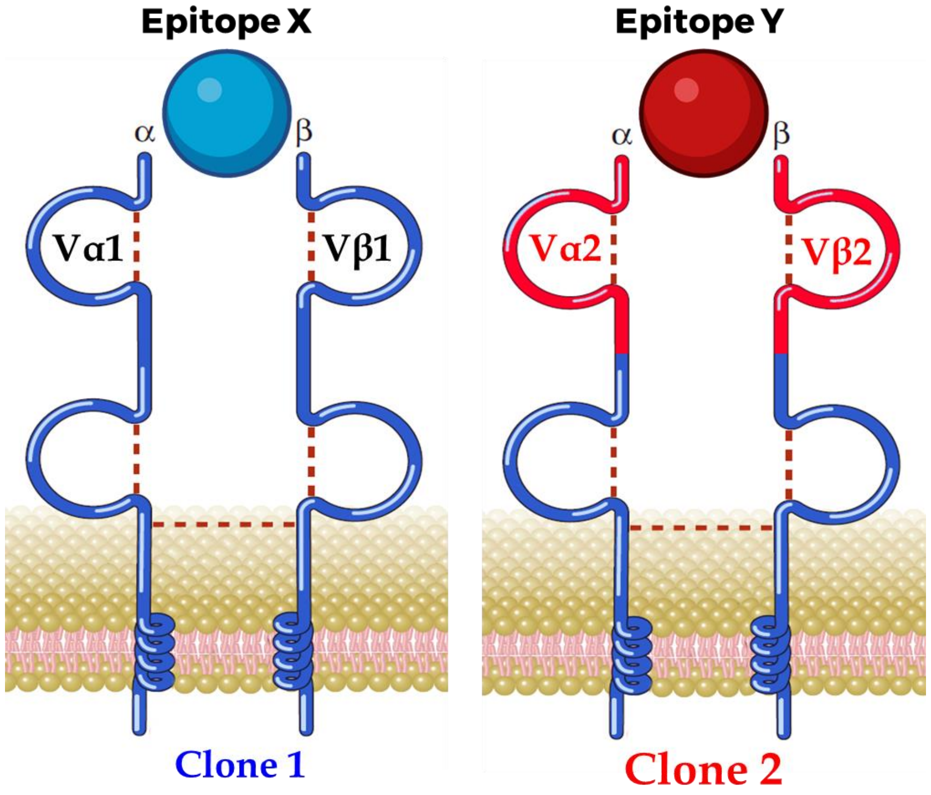
Each T cell clone **expresses TCR specific for 1 epitope**

↓

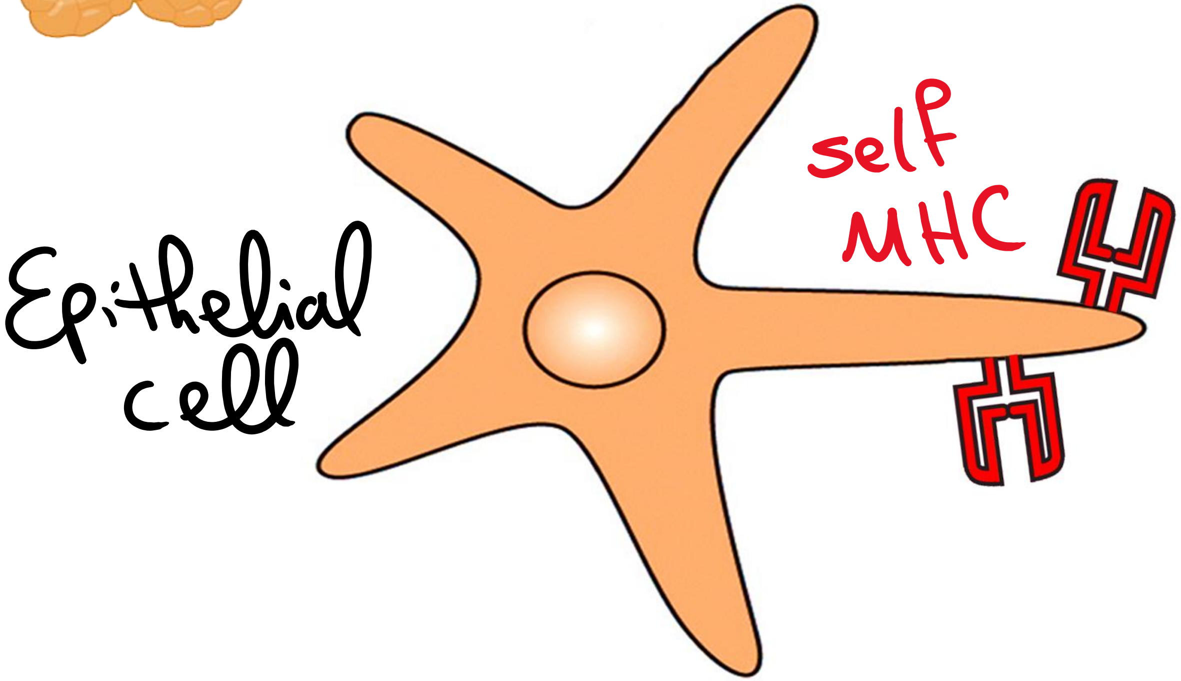
Millions of T cells clones with different TCR (differ in Vα & Vβ)

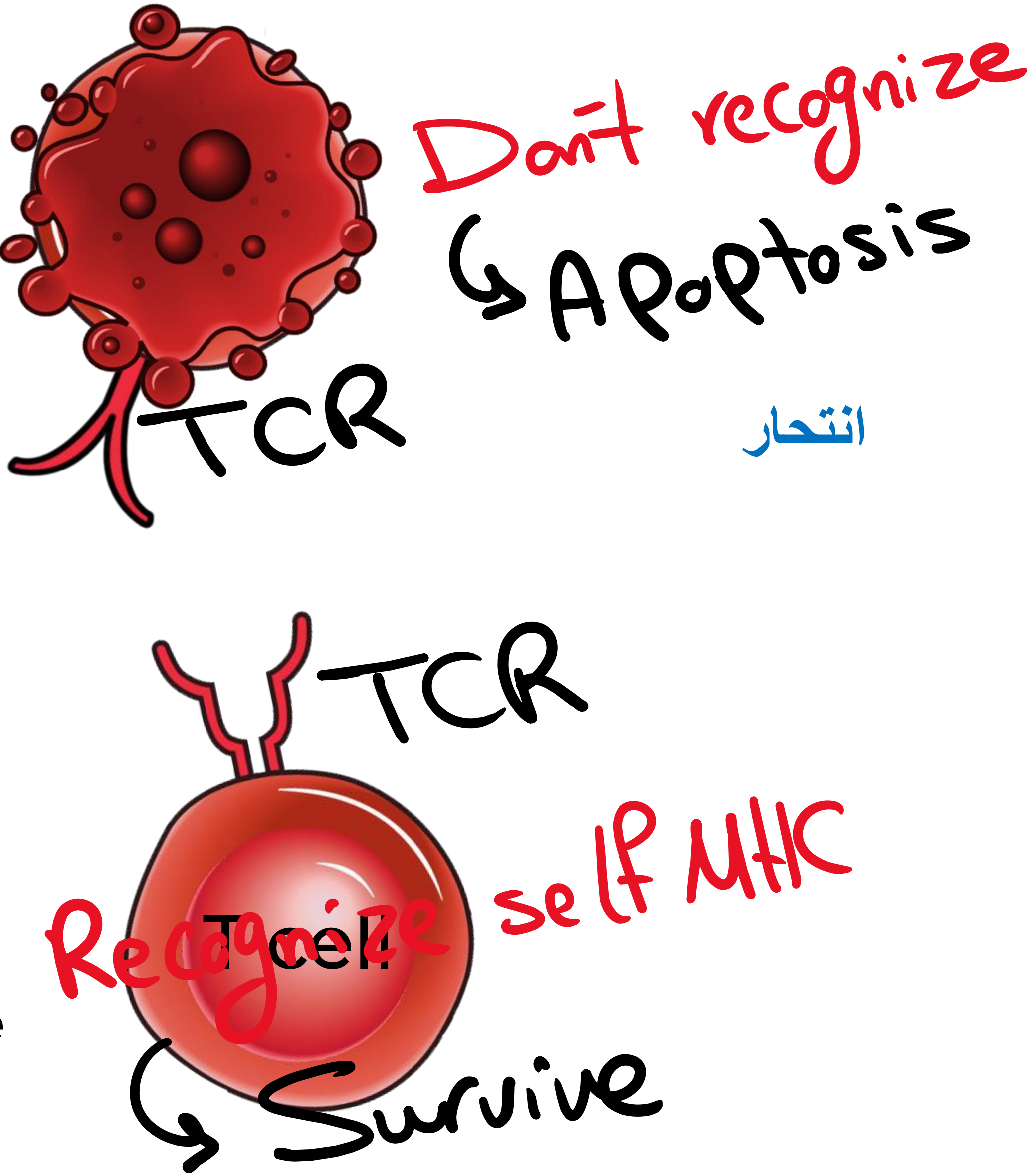
↓

Can react with **millions of different epitopes**



B Positive selection : اختيار ايجابي :تختار كلون لتحفزها





- T cells expressing TCR that **recognizes** **self MHC molecule** → **selected to survive**
- T cells which **don't recognize** **self MHC molecule** → **die by neglect**

Ⓒ Negative selection

T cells expressing **TCR that recognizes self peptide (self reactive clones) are deleted by apoptosis**

↓

Tolerance to self peptides (self tolerance)

↓

No autoimmune reaction

Positive & negative selection are called thymic education

Release from thymus

- **Mature T cells are of 2 types :**

1) T helper (CD4+ cells)

Constitute **65%** of circulating T cells

↓

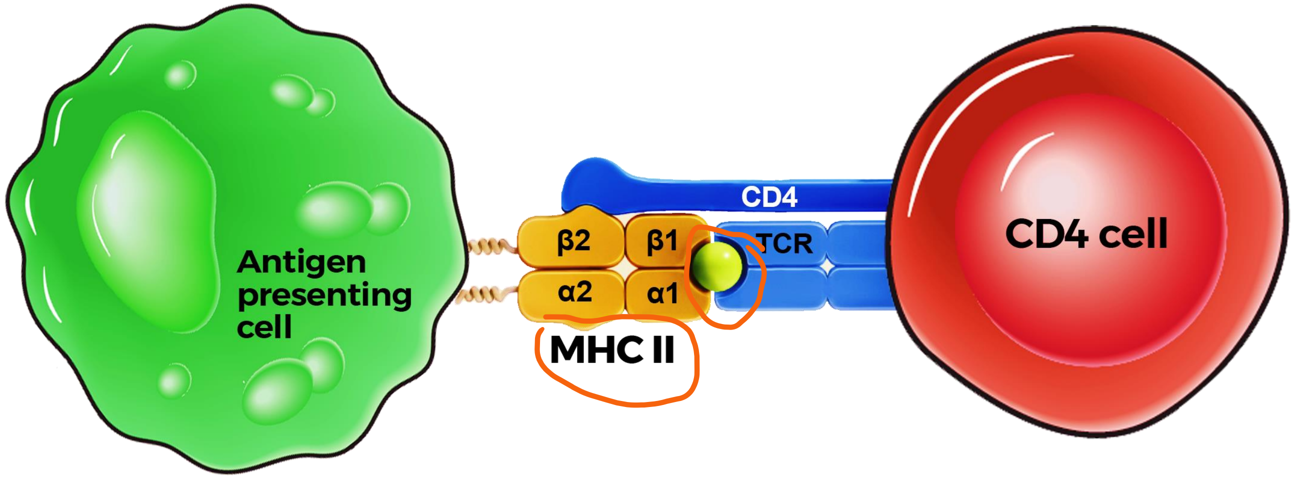
Recognize foreign Ag
in association with self MHC class II

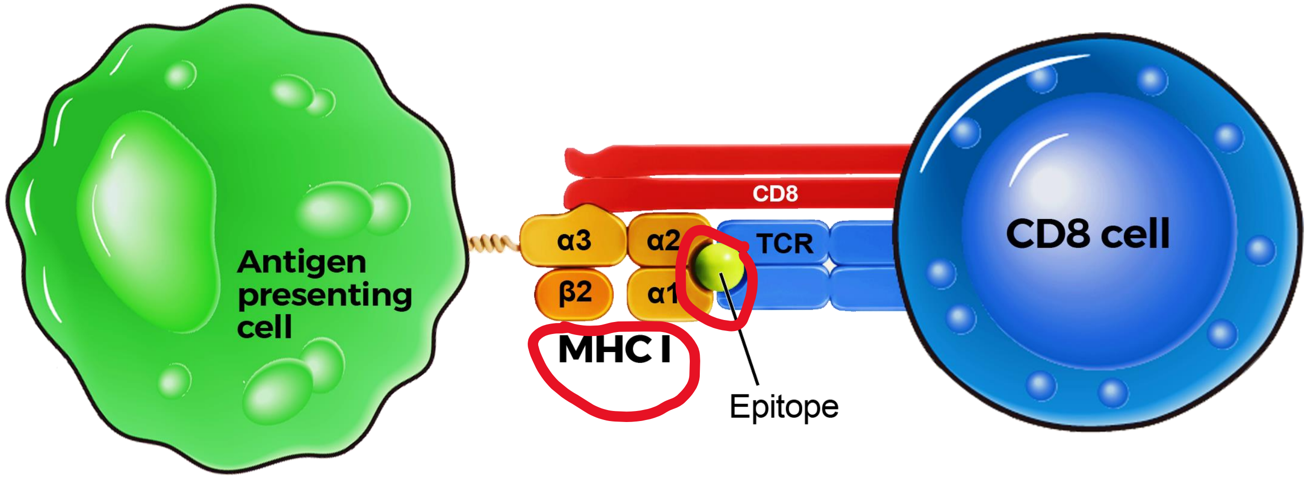
2) T cytotoxic (CD8+ cells)

Constitute **35%** of circulating T cells

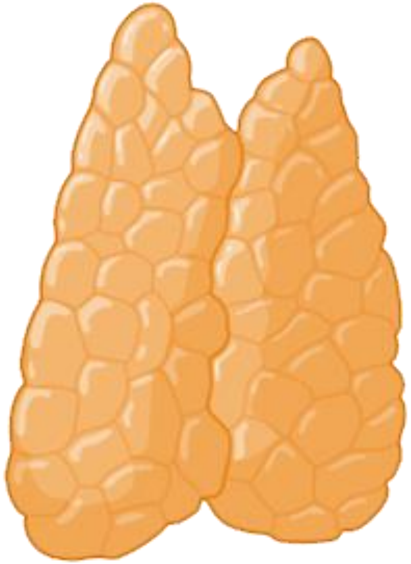
↓

Recognize foreign Ag
in association with self MHC class I





Release from thymus



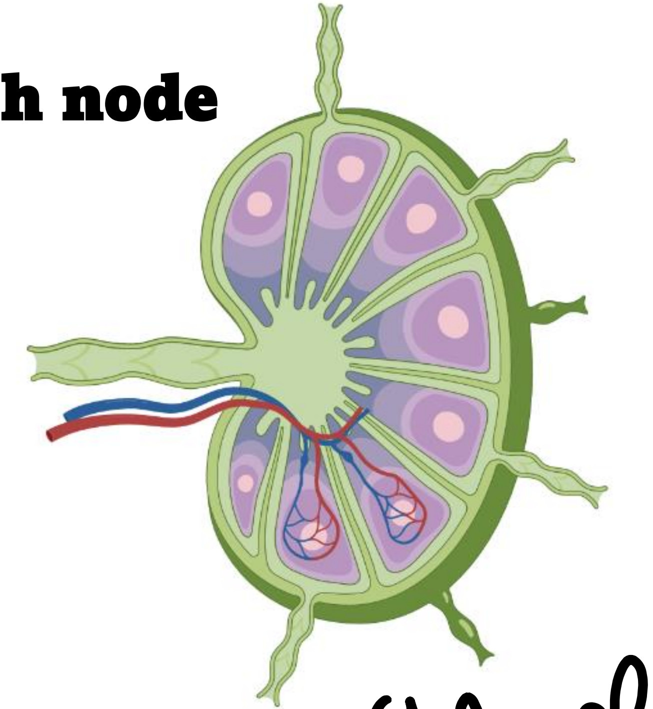
Mature T cells released from the thymus & **migrating to 2ry lymphoid organs :**

Are called **naive lymphocytes** (**mature that have never encountered Ag**)

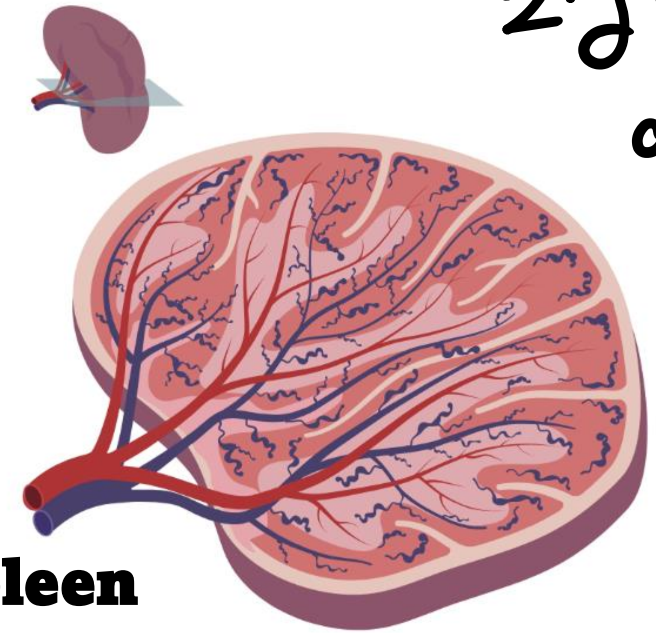
ساذجة Naive

ناضجة لم تقابل Ag

Mature T cell



2ry lymphoid organs



Quiz 2

T cells released from thymus recognize which of the following?

a. Self Ag in association with self MHC

b. Self Ag in association with foreign MHC

c. Foreign Ag in association with self MHC

d. Foreign Ag without MHC.

e. Self Ag without MHC

C